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| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 10/716,430  | 11/20/2003  | Masanobu Sugawara    | 011392A             | 6955             |
| 38834   | 7590        | 01/27/2006           | EXAMINER            |                  |
| WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP<br>1250 CONNECTICUT AVENUE, NW<br>SUITE 700<br>WASHINGTON, DC 20036 |             |                      | FREISTEIN, ANDREW B |                  |
|   |             | ART UNIT             | PAPER NUMBER        |                  |
|   |             |                      | 1626                |                  |

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                     |                 |
|------------------------------|---------------------|-----------------|
| <b>Office Action Summary</b> | Application No.     | Applicant(s)    |
|                              | 10/716,430          | SUGAWARA ET AL. |
|                              | Examiner            | Art Unit        |
|                              | Andrew B. Freistein | 1626            |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 08 November 2005.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) 1-44 and 50-68 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 45-49 and 69 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. 09/926,346.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 11/20/03.
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. 12282005.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

Claims 1-25, 35-69 are currently pending in the instant application. Claims 26-34 were cancelled by amendment.

### ***Priority***

This application is a Divisional Application of US Application No. 09/926,346, which granted as US Pat. No. 6,720,449, which was a 371 of PCT/JP01/01132, filed 02/16/2001. Acknowledgement is made of Applicant's claim for foreign priority under 35 U.S.C. § 119(a)-(d), by Japanese Patent Application No. P2000-039415, filed on 02/17/2000 and Japanese Patent Application No. P2000-334391, filed on 11/01/2000.

### ***Information Disclosure Statement***

Applicant's information disclosure statement (IDS), filed on 11/20/2003, has been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

### ***Response to Restriction Requirement***

Acknowledgement is made of Applicant's election (with traverse) of Group VIII, claims 48-49, in a response filed 11/08/2005.

Applicant traverses the restriction arguing that Group VII, claims 45-47 should be rejoined with the elected group. Examiner rejoins claims 45-47 and newly added claim 69 to Group VIII for examination.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

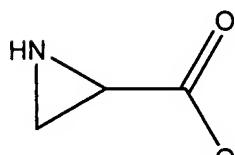
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**Claim 69** is rejected under 35 U.S.C. 102(b) as being anticipated by Mita et al, "Method for Preparation of Aziridine-2-Carboxylic Acid Salts", Japanese Kokai Patent Application No. Sho 57[1982]-146751.

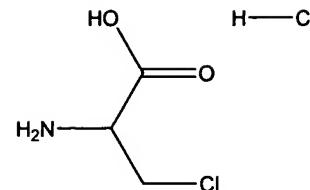
**Claim 69** is drawn to a process for producing an optically active aziridine-2-carboxylic acid derivative or its salt comprising using an optically active 3-haloalanine of formula (1) or its salt and performing an intramolecular cyclization reaction in the presence of a base to give an active aziridine-2-carboxylic acid derivative of formula (2).

Mita et al. disclose a method for preparation of aziridine-2-carboxylic acid salts, characterized in that  $\beta$ -haloalanines, their esters, or mineral acid salts are treated with alkali metal or alkaline earth metal hydroxide or ammonia water in water or a water-containing organic solvent (see McElroy Translation, "Claim," p. 1).

First, Mita et al. prepared aziridine-2-carboxylic acid sodium salt,



$\text{Na}^+$ , comprising: (1) dissolving sodium hydroxide in water; (2)

  
dissolving  $\beta$ -chloro- $\alpha$ -aminopropionic acid hydrochloride, , in  
water; (3) dropwise adding the first solution to the second solution under stirring; and (4)  
reacting the solutions at room temperature for 24 hours. (see McElroy Translation,  
"Application example 1," p. 5).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all  
obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148  
USPQ 459 (1966), that are applied for establishing a background for determining  
obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating  
obviousness or nonobviousness.

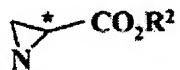
Claims 45-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over  
Mita et al, "Method for Preparation of Aziridine-2-Carboxylic Acid Salts", Japanese  
Kokai Patent Application No. Sho 57[1982]-146751.

The instant invention is drawn to a process for preparing optically active amino acid derivative or its salt.

**Claims 45-47** are drawn to a process for preparing optically active amino acid derivative or its salt comprising using an optically active 3-haloalanine derivative of



formula (1), , wherein X is halogen and R<sup>1</sup> is H or a monovalent organic group; \* represents the position of an asymmetric carbon atom; or its salt in the presence of a base to give an optically active aziridine-2-carbocyclic acid derivative of

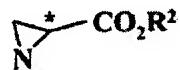


formula (2), , wherein R<sup>2</sup> and \* are defined in formula (1); characterized by using an alkali metal hydroxide or an alkaline earth metal hydroxide as the base, performing an intramolecular cyclization reaction in the presence of water at a temperature of 70°C or higher.

**Claims 48-49** are drawn to a process for preparing optically active amino acid derivative or its salt comprising using an optically active 3-haloalanine derivative of



formula (1), , wherein X is halogen and R<sup>1</sup> is H or a monovalent organic group; \* represents the position of an asymmetric carbon atom; or its salt in the presence of a base to give an optically active aziridine-2-carbocyclic acid derivative of

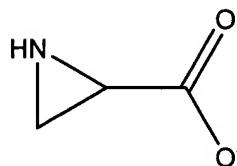


formula (2), , wherein R<sup>2</sup> and \* are defined in formula (1); characterized by using an amine as the base, performing an intramolecular cyclization reaction.

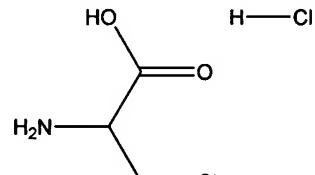
Determining the Scope and Content of the Prior Art

Mita et al. disclose a method for preparation of aziridine-2-carboxylic acid salts, characterized in that  $\beta$ -haloalanines, their esters, or mineral acid salts are treated with alkali metal or alkaline earth metal hydroxide or ammonia water in water or a water-containing organic solvent (see McElroy Translation, "Claim," p. 1). The reaction temperature range is 0-100°C (see McElroy Translation, p.4, para. 2).

First, Mita et al. prepared aziridine-2-carboxylic acid sodium salt,



$\text{Na}^+$ , comprising: (1) dissolving sodium hydroxide in water; (2)



dissolving  $\beta$ -chloro- $\alpha$ -aminopropionic acid hydrochloride, , in water; (3) dropwise adding the first solution to the second solution under stirring; and (4) reacting the solutions at room temperature for 24 hours. (see McElroy Translation, "Application example 1," p. 5).

Second, Mita et al. prepared aziridine-2-carboxylic acid potassium salt comprising: (1) dissolving potassium hydroxide in water; (2) dissolving  $\beta$ -chloroalanine hydrochloride in water; (3) adding the first solution dropwise to the second under stirring; and (4) heating the reaction solution to 60°C and react the solutions at 60-65°C for 4 hours (see McElroy Translation, "Application example 2," p. 5-6).

Third, Mita et al. prepared aziridine-2-carboxylic acid sodium salt in the same manner as example 1 except using  $\beta$ -chloroalanine methyl ester instead of  $\beta$ -chloroalanine hydrochloride (see McElroy Translation, "Application example 3," p. 6).

Fourth, aziridine-2-carboxylic acid calcium salt was prepared in the same manner as example 2, except calcium hydroxide was used in place of potassium hydroxide and excess calcium hydroxide was filtered out after the reaction (see McElroy Translation, "Application example 4," p. 6).

Fifth, aziridine-2-carboxylic acid sodium salt was prepared by (1) dissolving sodium hydroxide in water; (2) dissolving  $\beta$ -chloroalanine hydrochloride in a mixed solvent comprising water and methanol; (3) slowly adding the first solution to the second solution dropwise under stirring; (4) heating the reaction mixture to 60°C and reacting at 60-65°C for 6 hours; and (5) distilling the reaction mixture at a reduced pressure to remove the methanol (see McElroy Translation, "Application example 5," p. 6).

Ascertaining the Differences Between the Prior Art and the Instant Application

Claims 45-47 are drawn to a process wherein the reaction temperature is 70°C or higher. The prior art discloses examples of reactions where the temperature is 60-65°C. However, the disclosure states that the reaction temperature range is 0-100°C and preferably 20-80°C (see McElroy Translation, p. 4, 2<sup>nd</sup> paragraph).

Claims 48-49 are drawn to a process wherein the base is an amine. The prior art examples are drawn to a reaction in which the base is sodium hydroxide, potassium hydroxide or calcium hydroxide as the base. However, the disclosure states that the base can be ammonia water (see McElroy Translation, p. 3, 3<sup>rd</sup> full paragraph). Amines

are organic derivates of ammonia in the same way that alcohols and ethers are organic derivates of water and are not patentably distinct.

*Finding Prima Facie Obviousness*

In the claims 45-47, the difference between the instant application and the prior art is the temperature at which the reaction occurs. Since the prior art discloses the temperature range that the instant claims are drawn to, one of ordinary skill in the art would be motivated to perform the reaction in the temperature range that would produce the desired result.

In claims 48-49, the difference between an amine and ammonia is slight. A primary amine is  $\text{RNH}_2$  and ammonia water is  $\text{NH}_3 \cdot \text{H}_2\text{O}$ , wherein the N has two lone electrons. One of ordinary skill in the art would recognize that ammonia,  $\text{NH}_4\text{OH}$ , is a derivative of amine and be motivated to use an amine rather than ammonia to prepare a higher yield. See *Ex parte Bluestone*, 135 USPQ 199 (1961).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

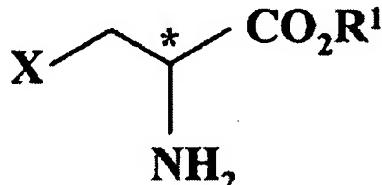
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 45-49 and 69 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 45 and 48 define  $\text{R}^1$  to represent "a hydrogen atom or a monovalent organic group which is involved in a structure represented by  $\text{O}_2\text{R}^1 \dots$ " A monovalent organic group can be any chemical with one bond to the Oxygen atom.  $\text{R}^1$  must be

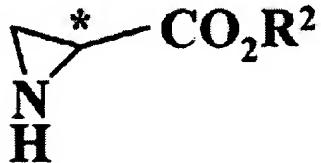
amended with a precise definition. The rejection can be overcome with a definition of  $R^1$  found in the specification such as: H, an alkyl group, or an aralkyl group.

Claim 69 is rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as his invention, because claim 69 fails to define formula (1) and formula (2).



Examiner presumes formula (1) is

and formula (2) is:



In order to overcome this rejection, claim 69 must recite the formula identified and the definitions of variables X,  $R^1$  and  $R^2$  similar to claims 45 and 48 with the amendments proposed in the rejection outlined above.

#### ***Claim Objections***

The abstract of the disclosure is objected to because it contains two paragraphs. The abstract should be in narrative form and generally limited to a single paragraph within the range of 50 to 150 words. Correction is required. See MPEP § 608.01(b).

#### ***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M<sup>c</sup>Kane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

KAMALA SAEED, PH.D.  
PRIMARY EXAMINER

  
\_\_\_\_\_  
Joseph K. M<sup>c</sup>Kane  
Supervisory Patent Examiner, AU 1626  
Date: January 23, 2006

Andrew B. Freistein  
Patent Examiner, AU 1626